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| EXAMINER | |
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| SAJJADI, FEREYDOUN GHOTB | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

***ADVISORY ACTION-CONTINUATION SHEET***

Continuation of 11. does NOT place the application in condition for allowance because: the examiner maintains the rejection of claims 1-4, 6-16, 29, 32-34, and 37, under 35 U.S.C. 103(a) as being unpatentable over Papahadjopoulos et al. (U.S. Patent No.: 6,803,053), taken with Rolland (U.S. Patent No.: 6,040,295), and further in view of Lunsford (U.S. Patent Publication No.: 2002/0182258); and the rejection of claims 1-4, 6-16, 26, 29, 32-34, and 37, under 35 U.S.C. 103(a) as being unpatentable over Papahadjopoulos et al. (U.S. Patent No.: 6,803,053), taken with Rolland, and further in view of Mathiowitz (U.S. Patent No.: 6,677,313), as set forth on pp. 2-4 of the final office action January 24, 2008, for reasons of record. Applicants' arguments have been fully considered, but are not found persuasive.

Applicants traverse the rejections, and argue that Papahadjopoulos describes cationic lipid:nucleic acid complexes containing, among other components: (a) a cationic lipid; (b) a nucleic acid; and (c) a hydrophilic polymer, and the reason for a hydrophilic polymer such as PEG-DSPE to be incorporated into a its cationic lipid:nucleic acid complexes is for the purpose of preventing the complexes from aggregating during storage and, increasing the shelf life of the complexes; and the skilled person would not have had any reason to entrap a PEG-DSPE-containing complex disclosed in Papahadjopoulos within a microparticle described in Lunsford or Mathiowitz.

In response, it should be noted that the primary reference is that of Papahadjopoulos et al., disclosing lipidic microparticles linked to targeting moieties (Abstract), prepared by contacting a nucleic acid with an organic polycation and an amphiphilic cationic lipid and then combining the complex thus formed with a hydrophilic polymer, that may be PEG-DSPE (columns 3 and 4 bridging). The reason for inclusion of a hydrophilic polymer such as PEG-DSPE in the microparticle is expressly provided by the primary reference. Lunsford claims (section 21, claim 1), a microparticle comprising a polymeric matrix, a lipid and a nucleic acid molecule that is not encapsulated. A person of ordinary skill in the art would not need to incorporate the components of the microparticle of Papahadjopoulos et al., into those of Lunsford or Mathiowitz. Rather the references of Lunsford and Mathiowitz were used to supply the

deficiencies in Papahadjopoulos et al. relating to microparticle diameter and antigenic peptide for delivery to mucosal tissue. As previously stated, for the purpose of combining references under 35 U.S.C. 103(a), the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The rejection of claims 21-24, 26-28, and 31 under 35 USC 103(a) as being unpatentable over Lunsford (U.S. Patent Publication No.: 2002/0182258), in view of Papahadjopoulos et al. (U.S. Patent No. 6,803,053), as set forth on pp. 4-5 of the final office action dated January 24, 2008 is maintained for reasons of record.

Applicants traverse the rejection, arguing Lunsford does not describe including in a microparticle a lipid (such as PEG-DSPE) having a pKa of less than about 2.5; and Papahadjopoulos would not have provided the skilled person any reason to include PEG-DSPE in a microparticle of Lunsford. Such is not found persuasive, because, Lunsford et al. do not limit the lipid components of their microparticle to a cationic lipid. Lunsford et al. disclose a preparation of microparticles for delivery of nucleic acids comprising a polymeric matrix, a nucleic acid expression vector, and a lipid, wherein the microparticles have a diameter less than about 100 microns (Abstract and Title). Lunsford et al. state that the lipid may be a cationic lipid or a phospholipid, thus providing the motivation to incorporate any cationic lipid or phospholipids in their polymeric matrix to form a microparticle. As previously indicated the pKa of less than about 2.5 is an inherent characteristic of PEG-DSPE.

The claim rejections are thus maintained in view of the foregoing commentary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633

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